

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	E-cigarette use and combustible tobacco cigarette smoking uptake among non-smokers, including relapse in former smokers: umbrella review, systematic review and meta-analysis
AUTHORS	Baenziger, Olivia; Ford, Laura; Yazidjoglou, Amelia; Joshy, Grace; Banks, Emily

VERSION 1 – REVIEW

REVIEWER	Deborah Black The University of Sydney, Australia
REVIEW RETURNED	10-Nov-2020

GENERAL COMMENTS	<p>This study adheres appropriately to guidelines for systematic reviews and meta-analyses. The statistics undertaken are appropriate but some of the results need to be addressed. In Figures 2,3 and 4, the authors list p values of 0.00. This indicates that there is no chance of making an error in making the inferences. There is always a chance of making an error and just because software indicates a p value of 0 to two decimal places does not mean it is correct.</p> <p>It would be preferable if 'data' were treated as plural.</p> <p>The primary research question is stated as "among current non-smokers, how does e-cigarette use affect the subsequent risk of smoking combustible tobacco cigarettes?". However, the prior systematic reviews have addressed this question. What is new in this study is that older populations are included and former smokers. Was this an aim or artefact of the literature search? If it is the later, than what is new about the research question? It needs to be made clear in the abstract and the research question.</p>
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REVIEWER	Ben Wamamili University of Canterbury, New Zealand
REVIEW RETURNED	12-Jan-2021

GENERAL COMMENTS	<p>E-cigarette use and combustible tobacco cigarette smoking uptake among non-smokers, including relapse in former smokers: umbrella review, systematic review and meta-analysis</p> <p>This manuscript reviewed and summarised current evidence on the uptake of cigarette smoking in non-smokers following e-cigarette use. The research reported in the manuscript is important for policy considerations on e-cigarette use globally. The manuscript is generally well written and communicated and many of my comments are minor.</p>
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ABSTRACT

- Design – please include ‘meta-analysis’ in the design (i.e. Design: Umbrella review, systematic review, and meta-analysis).
- Line 26-28: “Among former smokers, smoking relapse was higher in e-cigarette users versus non-users.” Did NRTs or other nicotine products/alternatives have any role here? Were there other important differences in characteristics of individuals who relapsed and those who did not relapse?

INTRODUCTION

- Page 4, lines 56-58 and page 5, lines 1-5: Evidence suggests that most people who report ever e-cigarette use do not graduate to regular/habitual use, and most vape out of curiosity. I recommend that this information be included to provide a balanced assessment of the issue (i.e. increasing e-cigarette use among never-smoking youth).
- It would be helpful to briefly comment on known risk factors for initiating e-cigarette use and how they relate with those for smoking initiation.

RESULTS:

Page 13, lines 37-49: I suggest that more information on the three studies be provided, particularly any inconsistencies. For example, study “[25]” reported lower odds of relapse among recent ex-smokers who vaped frequently or used advanced devices, and study “[46]” found very similar prevalence of relapse among recent quitters who never vaped (31.6%) and who vaped regularly (31.9%) compared with prior users (39.0%) and current occasional users (51.6%). This information would help the reader to make a balanced assessment of the evidence presented in this manuscript.

DISCUSSION:

- Page 14, lines 29-33: “The limited available evidence indicates that former smokers who use e-cigarettes have more than twice the odds of relapse and resumption of current smoking compared to former smokers who have not used e-cigarettes.” I recommend revising this statement (see my previous comment). For example, you could state: The limited available evidence indicates that former smokers who use e-cigarettes infrequently have higher odds of relapse.....
- Page 15, lines 2-4: Please see my comment in ‘Introduction’ about risk factors for smoking and vaping.

	<p style="text-align: center;">CONCLUSION</p> <p>Page 16, lines 29-31: “Intervention efforts and policies surrounding e-cigarettes are needed to reduce the potential of furthering combustible tobacco use in Australia.” I suggest revising this statement to reflect the wider (global) context of this paper. For example, “.....furthering combustible tobacco use in Australia and beyond.”</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Attached

Reviewer 1 comment 1: Design – please include ‘meta-analysis’ in the design (i.e. Design: Umbrella review, systematic review, and meta-analysis).

Author response: Meta-analysis has now been added to study design

Reviewer 1 comment 2: Line 26-28: “Among former smokers, smoking relapse was higher in e-cigarette users versus non- users.” Did NRTs or other nicotine products/alternatives have any role here? Were there other important differences in characteristics of individuals who relapsed and those who did not relapse?

Author response : This part of the meta-analysis compared relapse in past-smokers who did and did not use e- cigarettes. While some of the ex-smokers may also have used other NRT products, including both users and non-users of e-cigarettes, these data were not available. We agree this is an interesting question and have added the following to the text: “Data on use of other nicotine products by ex-smokers were not available.”

Reviewer 1 comment 3: INTRODUCTION: Page 4, lines 56-58 and page 5, lines 1-5: Evidence suggests that most people who report ever e-cigarette use do not graduate to regular/habitual use, and most vape out of curiosity. I recommend that this information be included to provide a balanced assessment of the issue (i.e. increasing e-cigarette use among never-smoking youth).

Author response: We agree with the reviewer and have now included specific reference to the frequency of use of e-cigarette in the introduction to reflect this:

“Evidence also suggests that most people who report ever e-cigarette use do not graduate to regular e-cigarette use [citations].”

In addition, ‘experimentation’ or ‘curiosity’ among youth is an important feature and has been included in the text as follows:

“E-cigarette use among youth is predominantly driven by curiosity and experimentation rather than smoking cessation [citations] ... Although the identification of risk factors for initiation of e-cigarette use are complex, it appears as though they are largely overlapping with those for smoking initiation [citations].”

Reviewer 1 comment 4:INTRODUCTION: It would be helpful to briefly comment on known risk factors for initiating e-cigarette use and how they relate with those for smoking initiation.

Author response : We have amended the manuscript to reflect on the evidence revealing shared risk factors for e-cigarette use and cigarette use, as follows:

“Although the identification of risk factors for initiation of e-cigarette use is complex, it appears as though many are similar to those for smoking initiation [citations]”

Reviewer 1 comment 5: RESULTS: Page 13, lines 37-49: I suggest that more information on the three

studies be provided, particularly any inconsistencies. For example, study “[25]” reported lower odds of relapse among recent ex- smokers who vaped frequently or used advanced devices, and study “[46]” found very similar prevalence of relapse among recent quitters who never vaped (31.6%) and who vaped regularly (31.9%) compared with prior users (39.0%) and current occasional users (51.6%). This information would help the reader to make a balanced assessment of the evidence presented in this manuscript.

Author response: This is interesting and we agree with the reviewer that it may be useful to report additional information about the studies. While we agree that vaping product characteristics are of potential interest, they were outside the pre-specified terms of the review. We have included information about the frequency of vaping and odds of relapse in the three studies in the results section as follows:

“Three [citations] newly-identified studies in this review investigated the odds of relapse to combustible cigarette smoking following the use of e-cigarettes in adults aged ≥ 18 years (Table 2). None of the three previously conducted systematic reviews investigated this relationship, so no additional studies from the umbrella review were included. Brose et al. used data from 371 adults who quit ≥ 2 months prior to baseline in 2016 from a national web-based survey in the UK [citation]. The other two studies used PATH data. Dai et al. looked at 3,210 ex-smokers, who had not smoked for >12 -months [citation]. McMillen et al. looked at data relating to 8,108 adults who had quit ≥ 5 years prior to baseline; sub-analyses from this study were included in the previous two sections, as the study also provided data on never smokers [citation].”

The comment regarding study 46 (Dai et al.) highlights a distinction between odds of relapse within 12 months versus long-term quitting. The percentages stated above are for recent (<12 month) quitters, while the adjusted odds ratio used in our research reflects the relapse in long term (>12 month) quitters (1.8% never, 10.4% prior, 9.6% current occasional and 15.0% current regular). As per our PROSPERO protocol, we chose the odds ratios to reflect the former smokers that had the longest time since cessation within each study. In Dai et al. this was the >12 -month group. The relevant text in the paper now reads:

“With respect to more detailed findings, in addition to the pre-specified meta-analyses, Brose et al. reported lower odds of relapse among recent ex-smokers who vaped daily versus those who vaped non-daily, while Dai et al. and McMillen et al. showed past 30-day regular e-cigarette use had greater odds of relapse than non-current use [citations]. Within the Dai et al. study, regular e-cigarette use in recent smokers (quit ≤ 12 months) was not associated with smoking relapse [citation] However, regular e-cigarette use in those who had ceased smoking for more than 12 months was associated with a significant increase in the odds of relapse.”

Reviewer 1 comment 6: DISCUSSION: Page 14, lines 29-33: “The limited available evidence indicates that former smokers who use e-cigarettes have more than twice the odds of relapse and resumption of current smoking compared to former smokers who have not used e-cigarettes.” I recommend revising this statement (see my previous comment). For example, you could state: The limited available evidence indicates that former smokers who use e-cigarettes infrequently have higher odds of relapse.....

Author response : The statement referred to here concerns the influence of e-cigarette use on ever relapse, regardless of frequency of use, rather than on a relationship between the frequency of e-cigarette use and relapse. For clarity we have therefore amended the sentence to:

“The limited available evidence indicates that former smokers who report current e-cigarette use within the previous 30-days have more than twice the odds of relapse and resumption of current smoking compared to former smokers who have not used e-cigarettes.”

Reviewer 1 comment 7: DISCUSSION: Page 15, lines 2-4: Please see my comment in ‘Introduction’ about risk factors for smoking and vaping.

Author response : This was addressed in our above response to comment 4

Reviewer 1 comment 8: CONCLUSION: Page 16, lines 29-31: "Intervention efforts and policies surrounding e-cigarettes are needed to reduce the potential of furthering combustible tobacco use in Australia." I suggest revising this statement to reflect the wider (global) context of this paper. For example, ".....furthering combustible tobacco use in Australia and beyond."

Author response : This suggested change has been made.

Reviewer: 2

Attached file

Reviewer 2 comment 1: This study adheres appropriately to guidelines for systematic reviews and meta-analyses. The statistics undertaken are appropriate but some of the results need to be addressed. In Figures 2,3 and 4, the authors list p values of 0.00. This indicates that there is no chance of making an error in making the inferences. There is always a chance of making an error and just because software indicates a p value of 0 to two decimal places does not mean it is correct.

Author response : The representation of p values has been changed to better reflect the results of statistical analysis, with p values previously labelled as 0.00 now reading ≤ 0.01 .

Reviewer 2 comment 2: It would be preferable if 'data' were treated as plural.

Author response : The text has been changed to correct for this.

Reviewer 1 comment 3: The primary research question is stated as "among current non-smokers, how does e-cigarette use affect the subsequent risk of smoking combustible tobacco cigarettes?". However, the prior systematic reviews have addressed this question. What is new in this study is that older populations are included and former smokers. Was this an aim or artefact of the literature search? If it is the later, than what is new about the research question? It needs to be made clear in the abstract and the research question.

Author response : We would like to thank this reviewer for this comment. This study had the intent to capture the risk of cigarette smoking in the broad population, including adults and former smokers. We have changed the text in the article to more explicitly reflect the new findings established by our review. The new question is phrased: "Among never smokers, current non- smokers and former smokers, how does e-cigarette use affect the subsequent risk of initiating use, current use and relapse to combustible tobacco cigarettes?"